

ORIGINAL ARTICLE

Intramuscular Risk at Insulin Injection Sites—Measurement of the Distance from Skin to Muscle and Rationale for Shorter-Length Needles for Subcutaneous Insulin Therapy

Laurence Hirsch, MD, Karen Byron, MS, and Michael Gibney, RN, MA

Abstract

Background: Intramuscular (IM) injection can increase insulin absorption, causing hypoglycemia. Available needle lengths today are 4–12.7 mm for pens and 6–12.7 mm for syringes. We describe the distance (D) from skin surface to muscle fascia at injection sites for subcutaneous (SC) insulin therapy and recommend needle lengths to reduce IM injection risk.

Materials and Methods: At two locations in the United States, skin and SC fat thicknesses were measured by ultrasound at the abdomen, arm, thigh, and buttock in diverse adults (body mass index [BMI] range, approximately 19–65 kg/m²) with diabetes ($n=341$ with one or more paired skin and SC measurement, permitting calculation of D). The natural log of D by body site, BMI, and gender were analyzed using a mixed model to estimate IM risk.

Results: D varied significantly by body site, BMI, and gender (each $P<0.001$), increasing with higher BMI and in women. Median D ranged from 10.9 mm (95% confidence interval, 10.3, 11.6) at the thigh to 16.9 mm (15.9, 18.1) at the buttock. Minimum D was <3 mm at the thigh and <5 mm elsewhere. When inserted 90° without pinch-up, the most commonly used needle worldwide (8 mm) has estimated IM risks of 25% and 9.7%, respectively, in the thigh and abdomen, versus 1.6% and 0.1%, respectively, with a 4 mm needle. A 45° insertion reduces, but does not eliminate, IM risk with longer needles.

Conclusions: Gender, BMI, and body site affect D ; when combined with needle length and insertion angle, these factors permit detailed estimates of IM insulin injection risk. Such risk varies across sites, appears greatest at the thigh, is unnecessarily increased with 8 mm and 12.7 mm needles, and is greatly reduced with shorter-length needles and good injection technique.

Introduction

THE DELIVERY TARGET FOR INSULIN is the subcutaneous (SC) tissue. Intramuscular (IM) insulin injection accelerates and increases insulin absorption and glucose-lowering activity, which are greatly affected by exercise of the injection site.^{1–5} Consistent delivery of insulin into the SC tissue helps reduce variability in absorption, glycemic profiles, and episodes of unanticipated hypoglycemia. Needle length is an important determinant of the depth of insulin deposition; needles 6 mm and longer have been shown to frequently reach the muscle when inserted straight in (at 90°, perpendicular to the skin) without the use of a skinfold.^{6–9} Clinician knowledge of skin and SC fat thickness is therefore essential for use of appropriate length needles for SC insulin delivery.

In our study of diverse adults with diabetes,¹⁰ we showed that skin thickness (ST) and SC fat thickness (SCT) vary in different ways at different insulin injection sites (abdomen, thigh, arm, buttocks). Mean ST is consistent, varying by <0.6 mm across injection sites and minimally by age, race, gender, body mass index (BMI), or diabetes type. However, SCT is much more variable and is increased with higher BMI, in women, and at the abdomen and buttocks versus the limbs. In our previous article, IM insertion risk was estimated in subjects with at least one paired ST–SCT measurement and *pooled* across all four injection sites, serving as a general indicator of the relationship between IM risk and needle length. As expected, potential IM injection risk rose from 0.4% to 45% for 4 mm to 12.7 mm needles, the range of insulin pen needles currently marketed.¹⁰ (Today, insulin syringe needle lengths range from 6 mm to

12.7 mm.) However, those estimates of IM risk have limited clinical value because there are substantial differences between injection sites for adipose thickness.

This new analysis provides clinically relevant data for each injection site. We now report the distance between the skin surface and muscle fascia (D) at each of the four injection sites, the impact of common demographic factors such as BMI and gender on D , and the *site-specific* estimates of potential IM injection risk. These data provide evidence to guide selection of the most appropriate needle length and injection technique for patients to perform consistent SC insulin delivery and to decrease inadvertent IM injections—for both insulin pens and syringes.

Patients and Methods

The study methods and primary results have been reported previously.¹⁰ In brief, 388 subjects with widely varying BMI and age >18 years with diabetes for ≥ 1 year had standardized ultrasound measurement of ST and SCT at insulin injection sites. Subject recruitment was enriched with obese persons to improve analysis of the relationship between high BMI and ST. The study was conducted at two sites in the United States (Rainier Clinical Research Center, Renton, WA; and Diablo Clinical Research, Walnut Creek, CA) in compliance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from each participant, and the protocol was approved by the Copernicus Group Institutional Review Board. Combining paired ST and SCT measurements ($n = 1,208$ for 341 subjects [both measurements could not be obtained at all injection sites]) allows calculation of D . Comparing D with nominal needle length for needles 4–12.7 mm, without lifting a skinfold or compressing skin, gives an estimate of the probability of IM injection, where needle length exceeds D . No needle insertions were performed in this study.

This report provides detailed information per body site. As the data distribution was skewed with a heavy right tail, the natural log of D , or $\ln(D)$, was used in a mixed model to evaluate the effect of body site, BMI, and gender on $\ln(D)$. Subject was included in the model as a random effect to account for the impact of repeated measures on individual subjects. D was then compared with effective needle length to estimate IM injection probability. Only summary statistics are provided for the estimates of IM injection, as this outcome is derived directly from comparison of needle length and the measured D .

Results

Demographics of the 341 subjects with at least one paired ST+SCT site measurement did not differ from the total study population (Table 1). The number of subjects with paired measurements at an injection site ranged from 338 for the thigh to 250 for the buttock. Median D from skin surface to muscle fascia is smallest at the thigh and largest at the buttock—a difference of 6.0 mm between the sites ($P < 0.001$) (Table 2). The absolute minimum D was also at the thigh (2.9 mm) and was < 5 mm at all sites. Similarly, maximum D was smallest in the thigh and similar for the arm, abdomen, and buttocks (approximately 42–47 mm). The range of D (minimum to maximum) varied from approximately 30 mm at the thigh to more than 42 mm at the abdomen, attributable primarily to variation in SCT.

TABLE 1. DEMOGRAPHICS OF THE STUDY POPULATION

Characteristic	Total	Current analysis
Number	388	341
Gender female	174 (44.8%)	155 (45.5%)
Race		
White/Caucasian	156 (40.2%)	139 (40.8%)
Asian	98 (25.3%)	78 (22.9%)
Black/African American	62 (16.0%)	56 (16.4%)
Hispanic/Latino	55 (14.2%)	52 (15.2%)
Other/two or more races	17 (4.4%)	16 (4.7%)
Diabetes type 2	280 (72.2%)	244 (71.6%)
Age (years)		
Mean (SD)	55.2 (13.4)	55.5 (13.4)
Minimum/maximum	18/85.6	18/85.6
Age category (years)		
18–39	59 (15.2%)	50 (14.7%)
40–59	175 (45.1%)	153 (44.9%)
≥ 60	154 (39.7%)	138 (40.5%)
Diabetes and insulin use (% of all subjects)		
Type 1	108 (27.8%)	97 (28.4%)
Type 2, no insulin	174 (44.8%)	159 (46.6%)
Type 2, insulin	106 (27.3%)	85 (24.9%)
BMI (kg/m^2)		
Mean (SD)	29.9 (7.1)	29.7 (7.0)
Minimum/maximum	19/65	19/62
BMI category (kg/m^2)		
< 25	114 (29.4%)	106 (31.1%)
25–29.9	110 (28.4%)	94 (27.6%)
≥ 30	164 (42.3%)	141 (41.3%)

Demographics shown for the original study subjects ($n = 388$) and the subset ($n = 341$) with at least one paired measurement of skin and subcutaneous adipose thickness at an injection site.

BMI, body mass index.

D increases directly with BMI ($P < 0.001$) and at the thigh ranges from 8.9 mm (95% confidence interval, 8.2, 9.6) in normal subjects to 13.3 mm (12.4, 14.2) in obese subjects ($P < 0.05$). At the abdomen, D ranges from 11.9 mm (11.0, 12.9) to 17.8 mm (16.6, 19.2) in normal and obese subjects, respectively ($P < 0.05$). D is consistently larger for women than men ($P < 0.001$). At the thigh, D averages 13.3 mm (12.5, 14.2) in women and 9.0 mm (8.4, 9.6) in men; at the abdomen, median D is 17.9 mm (16.7, 19.2) and 12.1 mm (11.3, 12.9) in women and men, respectively.

TABLE 2. DISTANCE FROM SKIN SURFACE TO MUSCLE FASCIA, BY BODY SITE FOR INSULIN INJECTION

Site	Number	Median (95% CI) (mm)	Minimum (mm)	Maximum (mm)
Thigh	338	10.9 (10.3, 11.6)	2.9	33.0
Arm	311	12.0 (11.3, 12.7)	4.1	43.8
Abdomen	309	14.7 (13.9, 15.6)	4.8	47.0
Buttock	250	16.9 (15.9, 18.1)	4.5	41.8

The distance from skin surface to muscle fascia was derived from adding paired thicknesses of skin and subcutaneous adipose tissue measured by high-frequency ultrasound at injection sites, in 341 subjects. The buttock is statistically thicker than the abdomen, which in turn is larger than the arm and thigh.

CI, confidence interval.

Estimates of IM injection risk (using the probability that needle length exceeds D) for different length needles and injection angle at the four injection sites are given in Table 3. IM risk is consistently highest at the thigh and lowest at the buttock, with the arm and abdomen intermediate. IM risk varies directly with needle length at each site. For the two most commonly used injection sites (abdomen and thigh),¹¹ the absolute reduction in IM risk between the shortest and longest pen needles (4 mm, 12.7 mm) inserted straight in (90°) exceeds 61 percentage points at the thigh and is nearly 38% at the abdomen—more than a 98% relative difference in both cases. For 6 mm and 12.7 mm needles—the range available for insulin syringes—absolute IM injection risk is reduced by >50 percentage points at the thigh and by >35 percentage points at the abdomen. With an 8 mm needle—the most common length used worldwide for insulin delivery for both syringes and pens¹¹—IM risk is 25% at the thigh, 2.5-fold greater than in the abdomen, and nearly fivefold greater than at the buttocks.

IM injection risk is substantially reduced with a 45° insertion angle, shown in Table 3. For needles 6–12.7 mm in length, the relative reductions for angled versus 90° insertions are nearly 50% with a 12.7 mm length in the thigh, 50% at the arm, and substantially greater reductions at other injection sites. At all sites, however, IM injection risk persists with a 45° insertion angle, particularly with 8 mm and 12.7 mm needles.

Estimated IM risks with 4–12.7 mm-length needles inserted at 90° are shown graphically by body site and both BMI and gender (Fig. 1), with specific risk estimates in Table 4.

TABLE 3. ESTIMATED INTRAMUSCULAR INJECTION RISK BY BODY SITE, NEEDLE LENGTH, AND INJECTION ANGLE

Needle length, injection angle	Thigh (n=338)	Arm (n=311)	Abdomen (n=309)	Buttock (n=250)
4 mm				
90°	1.6%	1.0%	0.3%	0.1%
45°	NA	NA	NA	NA
5 mm				
90°	4.7%	3.1%	1.1%	0.5%
45°	NA	NA	NA	NA
6 mm				
90°	10.0%	7.0%	2.8%	1.3%
45°	2.2%	1.3%	0.4%	0.2%
8 mm				
90°	25%	19.5%	9.7%	5.5%
45°	8.0%	5.5%	2.1%	1.0%
12.7 mm				
90°	63%	55%	38%	26.9%
45°	34%	27%	14.6%	8.8%

The probability of effective needle length exceeding the distance from the skin surface to muscle fascia is modeled, assuming insertions at 90° or at 45° angles, without lifting a skinfold or compressing skin. The effective needle length was calculated as $\cosine(90^\circ - \text{injection angle}) \times (\text{needle length})$. For example, the effective length of the 8 mm needle inserted at 90° is $\cosine(0^\circ) \times 8$ mm, or 8 mm; the effective length of the 8 mm needle inserted at 45° is $\cosine(45^\circ) \times 8$ mm, or 5.7 mm.

NA, not applicable. The recommended injection technique with 4 and 5 mm-length needles is 90° insertion without a skinfold in nearly all patients, other than very thin ones or young children, in whom a skinfold may be applied. Additionally, a 4 mm needle cannot be inserted at 45° because of physical characteristics of the needle length and hub.

Estimated IM risk is inversely related to BMI. Subjects with a BMI of <25 kg/m² have an approximately two- to fourfold greater IM risk compared with obese subjects at any injection site, regardless of needle length (Fig. 1). At the abdomen and thigh the 4 mm-length needle is estimated to have an IM risk of ≤4.5%, even in normal-weight subjects (men and women combined, Figure 1, bottom row). However, in subjects using 8 mm needles, the estimated risks for IM injections range from 41.4% at the thigh to 12.5% at the buttock in normal-weight subjects, compared with 14.0% and 2.2%, respectively, in obese subjects. In comparison, the estimated risks for the 12.7 mm needle at the abdomen and thigh are 55.5% and 77.9% in subjects with normal BMI, 36.2% and 61.0% in overweight subjects, and 23.4% and 46.2% in obese subjects, respectively.

Estimated IM risk is higher in men than women. Regardless of needle length or injection site, males are at approximately two- to fourfold greater IM risk than women (Figure 1, right column). In males, IM risk is estimated at 40.2% at the thigh with an 8 mm-length needle, compared with 13.8% in women. Across all injection sites, the 4 mm-length needle has estimated IM risks of <1% in all women and <5% in all males.

Discussion

Our analyses characterize the measured D from skin surface to muscle fascia at the four common insulin injection sites in diverse adults with diabetes, as well as the corresponding, wide-ranging estimated risks of IM needle insertions. With the thinnest ST and SCT (and therefore D), the thigh has the highest IM injection risk. At all body sites, men have higher risk versus women, and normal-weight subjects are likewise at greater risk than overweight or obese persons. As expected, IM risk is directly related to cannula length; needles of 8 mm and 12.7 mm length have unacceptably high risks for IM insertions.

Although median D ranged from approximately 11 to 17 mm at the thinnest (thigh) and thickest (buttocks) sites in our study, there was substantial variability, reflected in large ranges between minimum and maximum D within sites (approximately 30–42 mm), and marked differences in D between injection sites. Minimum D was <5 mm at all four injection sites and only 2.9 mm at the thigh (Table 2). These anatomic findings explain the potential for inadvertent IM insulin injection and the marked reductions with use of short needles.

The ranges in D (and IM injection risk) are largely related to differences in SCT across the common injection sites. Women have significant increases in SC adipose tissue (approximately 5 mm) compared with men, as do subjects with higher BMI—findings that are clinically relevant, as illustrated in the present report. The implications are that men and thinner subjects are at greater risk of inadvertent IM insulin injection than their obese counterparts or women, with highest risk in all patients consistently at the thigh (see Fig. 5 in Gibney et al.¹⁰), followed by the arm and the abdomen, with the lowest risks at the buttocks.

The thigh was reported as used by 59% of 4,300 insulin-injecting patients in a recent multinational survey,¹¹ making it the second most frequently used site for insulin injection after the abdomen. (In the same survey, 46–56% of adults, adolescents, and children reported using an 8 mm-length needle, making it the most commonly used length needle [pen and syringe] worldwide.¹¹) There are substantial differences

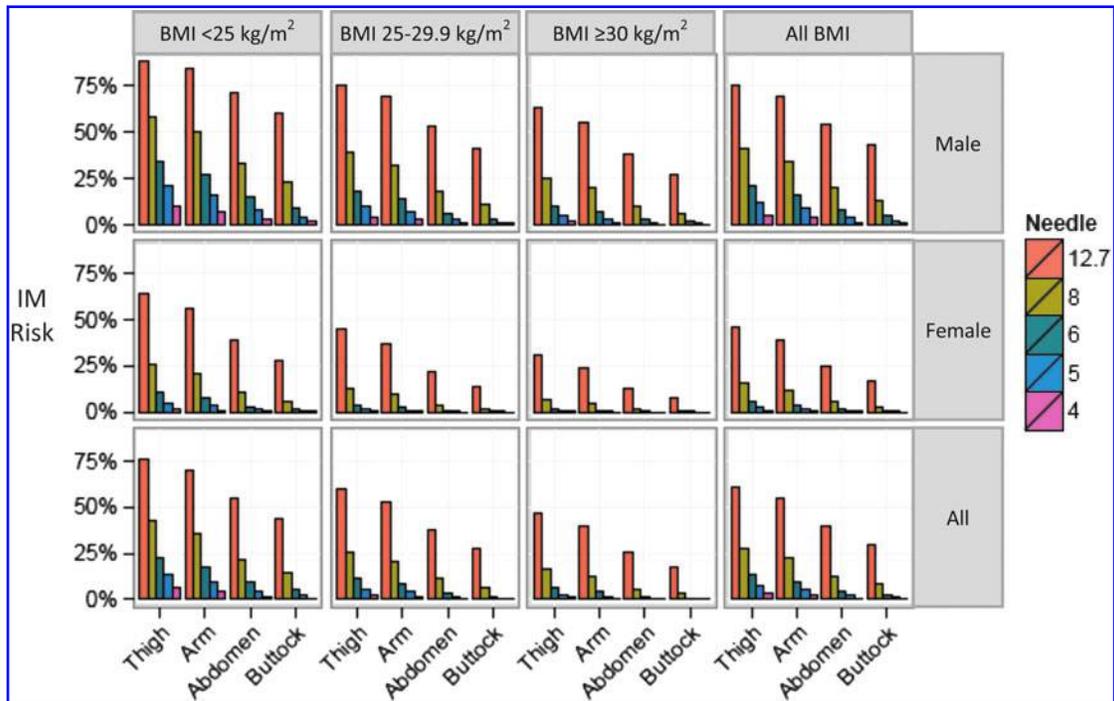


FIG. 1. Percentage intramuscular (IM) risk based on needle length, body site, body mass index (BMI), and gender. Estimated IM injection risk is provided based on comparisons of nominal needle length and combined thicknesses of skin and subcutaneous tissue measured at each injection site, assuming needle insertions at 90°, without lifting a skinfold. IM risk is present where needle length exceeds the sum of skin and subcutaneous thickness. Here, IM risk estimates are provided based on the two demographic factors shown to affect subcutaneous adipose tissue thickness—gender and BMI. (**Top row**) Males in normal, overweight, and obese BMI groups. (**Middle row**) Females in normal, overweight, and obese BMI groups. (**Bottom row**) All subjects by BMI group.

in estimated IM injection risk between these two commonly used body sites for all length needles. With the 8 mm-length needle at 90° insertion, IM injection risks are 2.5-fold higher at the thigh than the abdomen; for the 6 mm needle, the difference is nearly fourfold. With both needles, the estimated IM injection risks are lessened (but not eliminated) when using a 45° insertion, but the relative differences between body sites are even greater. Short needles—particularly 4 mm—reduce IM risk and may be used with a simpler, straight-in, one-handed injection technique by nearly all patients, which is easily taught by healthcare providers.

IM insulin injections should be a concern for both clinicians and patients with diabetes. Human insulins (regular+NPH) as well as analogs have shown *variably* accelerated kinetics when injected into muscle versus SC adipose tissue¹⁻⁴; the added effect of exercise can substantially heighten speed and unpredictability of insulin uptake and may lead to severe hypoglycemia.²⁻⁵ Consistent SC injection of insulin remains important to reduce glycemic variability. It is increasingly recognized that the longer insulin needle lengths used for decades (8 and 12.7 mm) cause IM injections in many patients.¹² Early work using ultrasound showed >80% IM injections in the thighs of normal-weight children with 12.7 mm needles; this was “improved” but was still nearly 30% with 8 mm needles.⁶ Such risks are further reduced with shorter needles—maximally by the 4 mm length for pens, but also by 6 mm needles for syringes—shown in this analysis.

IM injection of insulin can be advantageous when faster uptake and action are desired. Indeed, in the 1970s, IM injection of regular human insulin was demonstrated to be an

alternative approach to treatment of diabetic ketoacidosis—with similar effectiveness as traditional intravenous insulin infusion.^{13,14} Some patients may intentionally attempt to inject short-acting insulin IM when correcting transient high glucose values based on self-monitoring of blood glucose. However, the variability of the insulin uptake due to unpredictable exercise of the muscle tissue^{3,4} is neither desirable or practical for chronic ambulatory insulin therapy. With today’s narrower-diameter (higher-gauge) needle cannulas, patients may not recognize when they inject insulin IM and may or may not respond by partial withdrawal of the injection needle—this has not been studied systematically and would only add unnecessary complexity to proper SC injection technique.

Although clinicians should ensure all insulin-treated patients are well trained regarding proper injection technique, it is especially important if the thigh is used. Most patients using needles ≥6 mm in length must either inject at an angle and/or raise a skinfold (“pinch-up”) to effectively reduce IM risk; 4 and 5 mm pen needles are a safe and equally effective alternative.^{12,15-19} The persistent use of 8–12.7 mm needles for insulin therapy appears to be based on habit and clinical inertia, without any evidence of superior metabolic control or reduction in injection problems, such as leakage or backflow from the skin.^{8,12,15,16,19} Such needles are longer than is necessary for consistent SC drug delivery and offer no inherent advantage. Recent market research data indicate that about 55% of all pen needles used in the United States today are 8 and 12.7 mm; the percentages are even higher in countries such as Australia and Brazil (BD, data on file). This

TABLE 4. ESTIMATED INTRAMUSCULAR RISK FOR EACH INJECTION SITE BY NEEDLE LENGTH, ACCORDING TO GENDER AND BODY MASS INDEX

Site, needle length (mm)	Male			Female		
	BMI category (kg/m ²)			BMI category (kg/m ²)		
	<25	25–29.9	≥30	<25	25–29.9	≥30
Thigh (n)	46	53	65	49	37	61
12.7	88.3%	75.8%	62.8%	63.7%	44.4%	30.4%
8	58.1%	38.7%	25.5%	26.2%	13.0%	6.7%
6	34.1%	18.4%	10.1%	10.6%	4.1%	1.7%
5	21.2%	9.9%	4.8%	5.1%	1.7%	0.6%
4	10.1%	3.9%	1.6%	1.7%	0.5%	0.1%
Arm (n)	52	57	76	54	37	62
12.7	84.1%	69.4%	55.3%	56.3%	37.0%	24.0%
8	50.5%	31.6%	19.7%	20.4%	9.4%	4.5%
6	27.4%	13.7%	7.1%	7.5%	2.7%	1.1%
5	16.1%	6.9%	3.2%	3.4%	1.0%	0.4%
4	7.1%	2.5%	1.0%	1.1%	0.3%	0.1%
Abdomen (n)	48	52	72	48	32	57
12.7	71.2%	52.7%	38.0%	38.9%	22.0%	12.6%
8	33.4%	17.9%	9.8%	10.3%	3.9%	1.7%
6	14.9%	6.3%	2.8%	3.0%	0.9%	0.3%
5	7.6%	2.7%	1.1%	1.2%	0.3%	0.1%
4	2.8%	0.8%	0.3%	0.3%	0.1%	<0.1%
Buttock (n)	41	43	41	51	31	43
12.7	60.1%	40.7%	27.2%	28.0%	14.2%	7.4%
8	23.3%	11.1%	5.6%	5.8%	2.0%	0.7%
6	9.0%	3.3%	1.4%	1.5%	0.4%	0.1%
5	4.2%	1.3%	0.5%	0.5%	0.1%	<0.1%
4	1.4%	0.3%	0.1%	0.1%	<0.1%	<0.1%

Estimated intramuscular injection risk is present where nominal needle length exceeds the distance from the skin surface to muscle fascia, assuming needle insertions at 90°, without lifting a skinfold. Here, intramuscular risk is provided based on the two demographic factors that affect subcutaneous adipose tissue thickness: gender and body mass index (BMI). The *n* values given are the number of paired measurements of skin and subcutaneous thickness at each injection site, in each gender–BMI subgroup. For each length needle, highest intramuscular risks are at the thigh, and lowest are at the buttock. Men have increased risk compared with women, as do normal-weight subjects versus those who are overweight or obese.

has implications for all patients, not only those who are thin, who are children, or who inject in the limbs. The data likely apply to other drugs intended for SC delivery, such as growth hormone, parathyroid hormone, or heparin, and for continuous SC insulin pump catheters as well.

For patients using insulin syringes, needle lengths were limited to 8 mm and 12.7 mm for many years. Beginning in 2012, insulin syringes with a 6 mm-length needle became available and provide a lower risk of IM insertions. However, lengths shorter than this have not been marketed because of the need for users to reliably insert the syringe needle through the vial stopper and withdraw insulin (not a challenge for pen needles). A 6 mm-length needle is now the shortest needle on an insulin syringe.

Recent recommendations on injection technique strongly advise using shorter-length needles, including in adults.¹² Prospective, controlled trials (mostly crossover studies) comparing different length needles have consistently found equivalent glycemic control, less pain, and minimal “back-flow” or skin leakage with shorter lengths, which patients usually prefer.^{8,9,15–19} A randomized, controlled study confirmed these outcomes for a 4 mm×32 gauge pen needle, versus 5 mm and 8 mm×31 gauge needles, in adults with diabetes and BMI up to 49 kg/m²; a post hoc analysis showed equivalent glycemic control without increased skin leakage

for the 4 mm needle in the obese subjects, similar to the non-obese ones.^{16,20} A prospective randomized, controlled crossover study in obese patients (BMI up to 60 kg/m²) has been reported and confirms such findings for the 4 mm-length needle compared with both 8 mm- and 12.7 mm-length needles.²¹ Other studies have quantified skin leakage injections using needles as short as 4.5 mm and found only fractions of a unit of leakage (at most about 3.5% of the amount injected), even at injection volumes equivalent to 60 units—with the amount of leakage linked to dose, but not to needle length.^{22–24}

Many obese patients with type 2 diabetes have upper body segment fat distribution that is predominantly visceral; hence it cannot be assumed that there is excessive SC adipose tissue for injections in the thigh,^{25,26} where minimum *D* was only 2.9 mm in our population. Furthermore, three-quarters of patients reported they inject insulin at 90°, and one-fourth indicated they do not pinch up at the thigh.¹¹ Even with needles as short as 6 mm, a 45° insertion reduces, but does not eliminate, IM injection risk (Table 3), suggesting the need for raising a skinfold with the 6 mm-length needle.⁷ Lifting a skinfold requires proper technique and has variable effect—for thinner patients in one study, it actually reduced thigh SC thickness, serving to increase IM injection risk.⁷

Limitations of these analyses are that IM injection risk estimates are based on anatomic study; needle insertions

were not performed. Our highest estimates assume 90° insertions without lifting a skinfold; risk is reduced but not eliminated by 45° insertions. The IM risk estimates could not be adjusted for potential skin dimpling and fat tissue compression when excessive force is used with needle insertion—this may further increase risk. Nor could we quantify the impact of raising a skinfold, which can have variable impact on IM risk, as noted. The IM risk estimates also did not account for any variation from the nominal needle length—the analyses assumed all needles are exactly the labeled length. In addition, 42% of subjects studied had a BMI of >30 kg/m², and few subjects were thin—therefore the analyses may actually *underestimate* potential IM injection risk across the global patient population with diabetes. For instance, in Asia, type 2 diabetes develops at a much lower BMI than in the population we studied^{27,28}; shorter needles are clearly appropriate in such regions. Also, children and adolescents, who were not evaluated in this study, have slightly thinner skin^{29,30} and (usually) less SC fat than adults. Based on their study of ST and SCT in children and adolescents with type 1 diabetes, LoPresti et al.³⁰ strongly recommended 4 mm pen needles in such patients.

In summary, insulin should be delivered consistently to SC tissue. Based on improved understanding of skin and SCT at common injection sites, IM injection is a real risk with longer needles, including the current most widely used 8 mm length, particularly in the thigh. Clinicians, educators, and patients should carefully consider the desirability of this site for insulin injection. Use of a 4 mm pen needle and 6 mm needle syringe, along with good injection technique, can substantially reduce the risk of IM injection.

Acknowledgments

The authors thank the investigators and patients who volunteered to have their injection sites measured in this study. The authors also acknowledge the efforts of colleagues who contributed to the conduct of the study, including Christina Arce, Katie McNamara, and Dr. Kenneth Kassler-Taub.

Author Disclosure Statement

All the authors are employed by Becton, Dickinson & Co., Inc. and own shares or options to buy shares in BD.

L.H. conceived of this analysis, wrote the first draft of the manuscript, and revised it for substantive content. K.B. performed the statistical analysis and helped revise the manuscript. M.G. revised the manuscript and provided substantive input. All authors vouch for the integrity of the data.

References

1. Thow JC, Johnson AB, Fulcher G, et al.: Different absorption of isophane (NPH) insulin from subcutaneous and intramuscular sites suggests a need to reassess recommended insulin injection technique. *Diabet Med* 1990;7:600–602.
2. Karges B, Boehm BO, Karges W: Early hypoglycaemia after accidental intramuscular injection of insulin glargine. *Diabet Med* 2005;22:1444–1445.
3. Vaag A, Handberg A, Lauritzen M, et al.: Variation in absorption of NPH insulin due to intramuscular injection. *Diabetes Care* 1990;13:74–76.
4. Vaag A, Damgaard Pedersen K, Lauritzen M, et al.: Intramuscular versus subcutaneous injection of unmodified insulin; consequences for blood glucose control in patients with type 1 diabetes mellitus. *Diabet Med* 1990;7:335–342.
5. Frid A, Ostman J, Linde B: Hypoglycemia risk during exercise after intramuscular injection of insulin in thigh in IDDM. *Diabetes Care* 1990;13:473–477.
6. Tubiana-Rufi N, Belarbi N, Du Pasquier-Fediaevsky L, et al.: Short needles (8 mm) reduce the risk of intramuscular injections in children with type 1 diabetes. *Diabetes Care* 1999;22:1621–1625.
7. Hofman PL, Lawton SA, Peart JM, et al.: An angled insertion technique using 6-mm needles markedly reduces the risk of intramuscular injections in children and adolescents. *Diabet Med* 2007;24:1400–1405.
8. Schwartz S, Hassman D, Shelmet J, et al.: A multicenter, open-label, randomized, two-period crossover trial comparing glycemic control, satisfaction, and preference achieved with a 31 gauge×6mm needle versus a 29 gauge×12.7mm needle in obese patients with diabetes mellitus. *Clin Ther* 2004;26:1663–1678.
9. Birkebaek NH, Solvig J, Hansen B, et al.: A 4-mm needle reduces the risk of intramuscular injections without increasing backflow to skin surface in lean diabetic children and adults. *Diabetes Care* 2008;31:e65.
10. Gibney M, Arce C, Byron K, et al.: Skin and subcutaneous adipose layer thickness in adults with diabetes at sites used for insulin injections: implications for needle length recommendations. *Curr Med Res Opin* 2010;26:1519–1530.
11. De Coninck C, Frid A, Gaspar R, et al.: Results and analysis of the 2008–2009 Insulin Injection Technique Questionnaire survey. *J Diabetes* 2010;2:168–179.
12. Frid A, Hirsch L, Gaspar G, et al.: New injection recommendations for patients with diabetes. *Diabetes Metab* 2010;36(Suppl 2):S3–S18.
13. Alberti KGMM, Hockaday TDR, Turner RC: Small doses of intramuscular insulin in the treatment of diabetic 'coma.' *Lancet* 1973;302:515–522.
14. Sacks HS, Shahshahani M, Kitabchi AE, et al.: Similar responsiveness of diabetic ketoacidosis to low-dose insulin by intramuscular injection and albumin-free infusion. *Ann Intern Med* 1979;90:36–42.
15. Kreugel G, Keers JC, Kerstens MN, et al.: Randomized trial on the influence of the length of two insulin pen needles on glycemic control and patient preference in obese patients with diabetes. *Diabetes Technol Ther* 2011;13:737–741.
16. Hirsch L, Gibney M, Albanese J, et al.: Comparative glycemic control, safety and patient ratings for a new 4 mm×32G insulin pen needle in adults with diabetes. *Curr Med Res Opin* 2010;26:1531–1541.
17. Miwa T, Itoh R, Kobayashi T, et al.: Comparison of the effects of a new 32-gauge×4-mm pen needle and a 32-gauge×6-mm pen needle on glycemic control, safety, and patient ratings in Japanese adults with diabetes. *Diabetes Technol Ther* 2012;14:1084–1090.
18. Nagai Y, Ohshige T, Kaori A, et al.: Comparison between shorter straight and thinner microtapered insulin injection needles. *Diabetes Technol Ther* 2013;15:550–555.
19. Strauss K, Hannel I, McGonigle J, et al.: Ultra-short (5 mm) insulin needles: trial results and clinical recommendations. *Pract Diab Int* 1999;16:218–222.
20. Hirsch L, Gibney M, Li L, et al.: Glycemic control, reported pain and leakage with a 4mm×32G pen needle in

- obese and non-obese adults with diabetes: a post hoc analysis. *Curr Med Res Opin* 2012;28:1305–1311.
21. Bergenstal RM, Strock E, Peremislov D, et al.: Insulin therapy with a 4mm×32G pen needle vs larger needles in obese subjects [abstract]. *Diabetes* 2013;62(Suppl 1): A250.
 22. Wittmann A, Köver J, Kralj N, et al.: Insulin leakage value in relation to pen needle length and administered dose after subcutaneous injection. *Diabetes Technol Ther* 2010;12: 587–590.
 23. Hofman PL, Derraik JGB, Pinto TE, et al.: Defining the ideal injection techniques when using 5-mm needles in children and adults. *Diabetes Care* 2010;33:1940–1944.
 24. Ignaut DA, Fu H: Comparison of insulin diluent leakage postinjection using different needle lengths and injection volumes in patients with type 1 or type 2 diabetes mellitus. *J Diabetes Sci Technol* 2012;6:389–393.
 25. Gallagher D, Kelley DE, Yim J-E, et al.: Adipose tissue distribution is different in type 2 diabetes. *Am J Clin Nutr* 2009;89:807–814.
 26. Snijder MB, Dekker JM, Visser M, et al.: Trunk fat and leg fat have independent and opposite associations with fasting and postload glucose levels: the Hoorn study. *Diabetes Care* 2004;27:372–377.
 27. Sone H, Ito H, Ohashi Y, et al.: Obesity and type 2 diabetes in Japanese patients. *Lancet* 2003;361:85.
 28. Yoon K-H, Lee J-H, Kim J-W, et al.: Epidemic obesity and type 2 diabetes in Asia. *Lancet* 2006;368:1681–1688.
 29. Seidenari S, Giusti G, Bertoni L, et al.: Thickness and echogenicity of the skin in children as assessed by 20-MHz ultrasound. *Dermatology* 2000;201:218–222.
 30. Lo Presti D, Ingegnosi C, Strauss K: Skin and subcutaneous thickness at injecting sites in children with diabetes: ultrasound findings and recommendations for giving injection. *Pediatr Diabetes* 2012;13:525–533.

Address correspondence to:

Laurence Hirsch, MD

Diabetes Care
BD

1 Becton Drive

Franklin Lakes, NJ 07417

E-mail: laurence_hirsch@bd.com